Metabolic modeling of Streptomyces and its relatives

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Abstract

Streptomyces species are often referred to as "antibiotic factories" due to their ability to produce a large number of clinically important compounds. They belong to the order *Actinomycetales*, which is biologically very diverse, showing differences in genome size, pathogenicity, ecological niche, as well as in the ability of some of the species to produce various secondary metabolites.

This thesis starts by introducing the genus *Streptomyces* and its relatives and describing the modeling techniques used for analyzing their metabolic functions (Chapter 1). We explored the metabolic system of two antibiotic producing model bacteria, *Streptomyces coelicolor* (Chapter 2) and *Streptomyces clavuligerus* (Chapter 3), and computationally investigated their mechanism of antibiotic production. To understand how these antibiotic producing species are phylogenetically related to other species of the group *Actinomycetales*, we constructed a comprehensive phylogenetic tree, and established a generally usable robust approach to construct fully resolved phylogenetic trees from genome sequences (Chapter 4). Results of the phylogenetic study formed the basis for large-scale metabolic modeling, and we identified metabolic as well as topological commonalities and differences among members of the group (Chapter 5). Furthermore, by combining phylogenetic information with gene expression data we prioritized "orphan" genes of *Streptomyces coelicolor* for future experimental study (Chapter 6).

Finally, the thesis concludes by discussing the future use of our results and models and outlines some perspective for further research into the Systems biology of antibiotic producing microbes (Chapter 7).